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KILYK & BOWERSOX, P.L.L.C.
400 HOLIDAY COURT
SUITE 102
WARRENTON, VA 20186

EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/062,257	ITOH, KYOGO	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2007 and 17 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-123* is/are pending in the application.

4a) Of the above claim(s) *5,6,9-43,51-116 and 118-123* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7,8,44,45 and 117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 November 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/14/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant is reminded that Applicant is required under 37 C.F.R. 1.821(d) to amend the specification to list the appropriate SEQ ID NOS for sequences disclosed in the specification (for example, page 37 at Table 5 [SEQ ID NO: 10] and page 13 at line 20. It is noted by the Examiner with regard to the sequence DYLRSV that appears on pages 13 and 36 at the cited locations, said sequence is a subsequence of SEQ ID NO: 2, *i.e.,* amino acid residues 1-6, and said sequence may be identified thus).

It is noted by the Examiner that Applicant has amended the latter two locations as "(subsequence of SEQ ID NO: 2)", however, Applicant is required to amend the specification to disclose which amino acid residues of SEQ ID NO: 2 the subsequence is.

2. Applicant's amendments filed 3/1/07 and 11/17/06 are acknowledged and have been entered.

3. Applicant is reminded of Applicant's election with traverse of Group I drawn to the peptide having an amino acid sequence of SEQ ID NO: 1, and inducer of CTL thereof, vaccine thereof, and pharmaceutical composition thereof (claims 1, 3, 7 and 44) in Applicant's response filed 5/24/06

Claims 1-4, 7, 8, 44, 45 and 117 are presently being examined as they read on Groups I, II and III (SEQ ID NO: 1-3).

The following are new grounds of rejection necessitated by Applicant's amendment filed 3/1/07.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

a. Claims 3 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V.

Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed inducer of CTL recited in instant claims 3 and 4, wherein the said inducer *consists essentially of* a peptide of claim 1 or claim 2.

The instant claims encompass "inducers" of CTL that consist essentially of the peptide of claim 1 or claim 2, wherein said "inducers" include subsequences of the recited SEQ ID NO in claims 1 and 2 ("an" amino acid sequence of SEQ ID NO...), and including other undisclosed components ("consisting essentially of" a peptide of claim 1 or claim 2).

The specification discloses that SEQ ID NO: 11, 12 and 16 can be used as inducers for inducing CTL (page 16 at lines 5-25 and page 17 at lines 1-8).

The specification does not disclose the definition of "inducer."

By using the term consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A consisting essentially of' claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao,317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of" consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also MPEP § 2111.03. The claim as a whole, including all limitations found in the preamble(see Pac-Tec Inc. v. Amerace Corp., 903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention), the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. Lockwood,107 F.3d at 1572, 41 USPQ2d at 1966

The instant disclosure does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera, including any peptide or non-peptide of an "inducer." Since the disclosure fails to provide sufficient relevant identifying characteristics, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus as broadly claimed.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief that clinical results for the present application are published in Clinical Cancer Res. 1005, 11(16): 5900-5911 (copy supplied by Applicant) and clearly shows the superior clinical effect of the present invention.

It is the Examiner's position that the instant claims are drawn to an inducer of CTL that "consists essentially of" a peptide of claim 1 or claim 2, said peptide consisting of "an" amino acid sequence of one of the recited SEQ ID NO, rather than an inducer of CTL that consists of one of SEQ ID NO: 1, 2 or 3. It is the Examiner's position that adequate written description must be present in the instant specification.

As a side issue, the data in the said publication are for mixtures of peptides, some mixtures including one of SEQ ID NO: 1, 2 and/or 3 of the instant claims along with other tumor associated peptides from different tumor associated proteins, and a lack of correlation with immune responsiveness to said SEQ ID NO with clinical response since in some instances no immune response is noted to the said SEQ ID NO, but to other non-related peptides in the mixture, but clinical response is noted in terms of survival time for example, or in other instances, immune response is noted, but clinical outcome is not correlated positively with said response. In addition said publication states that "Increases in cellular or humoral responses specific to at least one of the vaccinated peptides were observed in the postvaccination samples of 15 of 21 patients regardless of the administration of prednisolone to the majority of patients. CTH responses were also observed in 12 of 21 patients. In contrast, no HLA class I-restricted cytotoxicity against glioma cells was observed, as measured by a 6-hour ^{51}Cr release assay, in either the prevaccination or the postvacination PBMCs. These results suggest that the administration of steroid hormone did not greatly influence the peptide-induced humoral responses, DTH responses, or cytokine production in response to an antigen, although it suppressed HLA class I-restricted cytotoxicity." (paragraph spanning pages 5909-5910). Said publication also teaches "Personalized peptide vaccinations were recommended for the further clinical study to malignant glioma patients." (abstract). In addition, said reference does not teach an internal positive control for HLA class I restricted CTL activity.

b. Claims 7, 8, 44 and 45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed pharmaceutical composition recited in instant claims 44 and 45, said pharmaceutical composition comprising an effective amount for cancer treatment of at least one peptide of claim 1 or claim 2, nor the cancer vaccine recited in instant claims 7 and 8, said cancer vaccine comprising at least the peptide of claim 1 or claim 2.

The instant claims encompass a pharmaceutical composition comprising an amount of at least one of the peptides of claim 1 or claim 2 effective for cancer treatment, or a cancer vaccine comprising the peptide of claim 1 or claim 2.

The specification discloses that SEQ ID NO: 1-3 are subsequence peptides of the lck protein that is over-expressed on adenocarcinoma cells or epithelial cancer cells in colon or small cell lung cancers bound to HLA-A2402, exhibited a CTL-activating ability of PBMC from a cancer patient (or PMBC from normal individuals when presented by HLA-A2402 on professional APC dendritic cells), as well as enhancing the production of IFN-γ by CTLs. The specification discloses that CTL induced by the said SEQ ID NO could recognize a tumor cell line (paragraph spanning pages 4-5, page 7 at lines 21-25, paragraph spanning pages 10-11, page 11 at lines 19-24, pages 12-13, Table 1 on page 28, Examples 4-6).

The specification further discloses that the amino acid sequence DYLRSV, common to both SEQ ID NO: 1 and 2, has a relevance to tumor rejection. The specification discloses searching for homologous sequences in other proteins, and testing subseqence 9-mer peptides from some of the tyrosine kinase proteins for binding to HLA-A2402 and for stimulating CTL (especially Examples 6-7). Larger 13-mer subsequences containing these peptides conform to the formula that is SEQ ID NO: 10 (Example 6).

There are no working examples of any *in vivo* method of treatment with the said peptide, and in addition, the specification does not provide adequate written description for "treating." The specification does not does not provide description that administration of the peptide produces such a CTL response that "treats."

The specification does not disclose working examples of any peptide recited in claim 1 or claim 2 used for treatment or for prophylaxis as a vaccine.

Evidentiary reference Marchand *et al* (Int. J. Cancer 20: 219-230, 1999, of record) teach "Considerable further progress is needed... before immunization with tumor-specific antigens recognized by T cells becomes an effective and generally applicable cancer therapy." (second to last sentence of article).

Evidentiary reference Marchand *et al* (Exp. Opin. Biol. Ther. 1(3): 497-510, 2001, of record) teach "It is fair to say that in patients vaccinated with defined antigen, the immune responses induced have been so far very poor, if present. In some studies, immune responses were reported for some patients but without any correlation with the clinical responses. In addition, some patients with complete and long-term regressions of several melanoma metastases failed to mount a detectable response against the antigen present in the vaccine." (last paragraph at column 2 on page 505).

Evidentiary reference Bodey *et al* (Anticancer Research 20: 2665-2676, 2000, of record) teach "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy (page 2665 at column 2). Bodey *et al* further teach "the use of active specific immunotherapy for cancer is still in its infancy despite several decades of clinical and basic research" (page 2668 at column 2).

Evidentiary reference Gao *et al* (J. Immunother. 23: 643-653, 2000, of record) found that although anti-tumor CTL response was enhanced by immunization, the tumors failed to regress due to an association with lack of CTL migration to the tumor sites (abstract). Thus, Gao *et al* teach that activation of peptide epitope-specific CTL is not an appropriate endpoint, and an estimation of efficacy based upon this factor is not predictive of actual efficacy of treatment *in vivo*.

Evidentiary reference Boon *et al* (Ann. Rev. Immunol. 2006, 24: 175-208) teach "Therapeutic vaccination of metastatic melanoma patients with these antigens [*i.e.*, melanoma antigens] is followed by tumor regressions in only a small minority of the patients (page 175, abstract). Boon *et al* further teach "In conclusion, therapeutic success following vaccination may not depend on the number of T cells produced directly by the vaccine, but rather on the production of a T cell clone with functional properties that enable it to migrate to the tumor and resist the local immunosuppressive environment long enough to initiate a regression process...To achieve therapeutic success, investigators will probably need to understand the cause of the local immunosuppression in the tumors and find counteracting agents. As stated above, the list of possible immunosuppressive agents present in tumors is considerable. But it will be important to find whether, for each type of tumor, there is a prevalent immunosuppressive agent. Just as many types of tumors have preferred oncogenic pathways that differ from one type of tumor to another, each type of tumor may also

have preferred immunosuppressive processes that we must identify to achieve therapeutic success...Therapeutic vaccination of cancer has not yet proved to be effective enough to become a generally applied cancer treatment...We do not believe that melanoma patients suffer from a degree of general immunosuppression, which we believe is restricted to very late-stage patients who are not included in most studies...Therefore, the difference in the quality of the response would be due to a chance event determining, for instance, the functional properties of the unique or the few responder T cell clones elicited by the vaccine. In that case, it will be essential to understand what this crucial functional property is. At the other extreme, the antivaccine T cell responses would be similar in all patients, but the level of resistance of the tumors would vary considerably. In that case investigators would need to identify the main component of this resistance and find ways to counteract it." (especially pages 193-194).

Evidentiary reference the Merck Manual (of record) teaches that a vaccine is a suspension of whole or fractionated bacteria or viruses that have been rendered nonpathogenic and is given to induce an immune response and prevent subsequent disease.

Evidentiary reference Encyclopedia Brittanica Online (of record) defines vaccine as a suspension of weakened, killed, or fragmented microorganisms or toxins or of antibodies or lymphocytes that is administered primarily to prevent disease.

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief that clinical results for the present application are published in Clinical Cancer Res. 1005, 11(16): 5900-5911 (copy supplied by Applicant) and clearly shows the superior clinical effect of the present invention.

It is the Examiner's position that the instant claims are drawn to a pharmaceutical composition recited in instant claims 44 and 45, said pharmaceutical composition comprising an effective amount for cancer treatment of at least one peptide of claim 1 or claim 2, nor the cancer vaccine, *i.e.,* a preventative composition, recited in instant claims 7 and 8, said cancer vaccine comprising at least the peptide of claim 1 or claim 2. It is the Examiner's further position that adequate written description must be present in the instant specification.

As a side issue, data in the said publication are for mixtures of peptides, some mixtures including one of SEQ ID NO: 1, 2 and/or 3 of the instant claims along with other tumor associated peptides from different tumor associated proteins, and a lack of correlation with immune responsiveness to said SEQ ID NO with clinical response since in some instances no immune response is noted to the said SEQ ID NO, but to other non-related peptides in the mixture, but clinical response is noted in terms of survival time for example, or in other instances, immune response is noted, but clinical outcome is not correlated positively with said response. In addition said publication states that "Increases in cellular or humoral responses specific to at least one of the vaccinated peptides were observed in the postvaccination samples of 15 of 21 patients regardless of the administration of prednisolone to the majority of patients. CTH responses were also observed in 12 of 21 patients. In contrast, no HLA class I-restricted cytotoxicity against glioma cells was observed, as measured by a 6-hour ^{51}Cr release assay, in either the prevaccination or the postvacination PBMCs. These results suggest that the administration of steroid hormone did not greatly influence the peptide-induced humoral responses, DTH responses, or cytokine production in response to an antigen, although it suppressed HLA class I-restricted cytotoxicity." (paragraph spanning pages 5909-5910). Said publication also teaches "Personalized peptide vaccinations were recommended for the further clinical study to malignant glioma patients." (abstract). In addition, said reference does not teach an internal positive control for HLA class I restricted CTL activity.

c. Claims 1-4, 7, 8, 44, 45 and 117 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed peptide consisting of "an" amino acid sequence of the SEQ ID NO recited in instant claim 1/inducer, vaccine recited in instant claim 7 or pharmaceutical composition thereof recited in instant claim 44, nor of the claimed peptide consisting of "an" amino acid sequence of SEQ ID NO: 10 recited in claim 2/kit comprising said peptide/inducer recited in instant claim 117, vaccine recited in instant claim 8 or pharmaceutical composition thereof recited in instant claim 45.

The instant claims encompass: (1) a peptide consisting of a subsequence of one of the SEQ ID NO recited in instant claim 1 ("an" amino acid sequence of SEQ ID NO....), said subsequence does not bind to HLA-A*2402 and elicit an immune response, and that in addition may comprise additional undisclosed flanking regions for the inducer of claims 3 and 4, (2) a peptide consisting of a subsequence of SEQ ID NO: 10 that is not one of SEQ ID NO: 1, 2, 4-9, but is rather a subsequence of SEQ ID NO: 10 that does not bind to HLA-A*2402 and elicit an immune response.

The specification discloses that SEQ ID NO: 1-3 are subsequence peptides of the lck protein that is over-expressed on adenocarcinoma cells or epithelial cancer cells in colon or small cell lung cancers bound to HLA-A2402, exhibited a CTL-activating ability of PBMC from a cancer patient (or PMBC from normal individuals when presented by HLA-A2402 on professional APC dendritic cells), as well as enhancing the production of IFN-γ by CTLs. The specification discloses that CTL induced by the said SEQ ID NO could recognize a tumor cell line (paragraph spanning pages 4-5, page 7 at lines 21-25, paragraph spanning pages 10-11, page 11 at lines 19-24, pages 12-13, Table 1 on page 28, Examples 4-6).

The specification further discloses that the amino acid sequence DYLRSV, common to both SEQ ID NO: 1 and 2, has a relevance to tumor rejection. The specification discloses searching for homologous sequences in other proteins, and testing subseqence 9-mer peptides from some of the tyrosine kinase proteins for binding to HLA-A2402 and for stimulating CTL (especially Examples 6-7). Larger 13-mer subsequences containing these peptides conform to the formula that is SEQ ID NO: 10 (Example 6).

There are no working examples of any smaller subsequences of SEQ ID NO: 1-3 that are shorter than 9 or 10 amino acid residues in length, or of subsequences of SEQ ID NO: 10 that do not contain one of SEQ ID NO: 1, 2, 4-9, and/or that contain additional undisclosed flanking amino acid sequence.

Evidentiary reference Marchand *et al* (Int. J. Cancer 20: 219-230, 1999, of record) teach "Considerable further progress is needed... before immunization with tumor-specific antigens recognized by T cells becomes an effective and generally applicable cancer therapy." (second to last sentence of article).

Evidentiary reference Marchand *et al* (Exp. Opin. Biol. Ther. 1(3): 497-510, 2001, of record) teach "It is fair to say that in patients vaccinated with defined antigen, the immune responses induced have been so far very poor, if present. In some studies, immune responses were reported for some patients but without any correlation with the clinical responses. In addition, some patients with complete and long-term regressions of several melanoma metastases failed to mount a detectable response against the antigen present in the vaccine." (last paragraph at column 2 on page 505).

Evidentiary reference Bodey *et al* (Anticancer Research 20: 2665-2676, 2000, of record) teach "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy (page 2665 at column 2). Bodey *et al* further teach "the use of active specific immunotherapy for cancer is still in its infancy despite several decades of clinical and basic research" (page 2668 at column 2).

Evidentiary reference Gao *et al* (J. Immunother. 23: 643-653, 2000, of record) found that although anti-tumor CTL response was enhanced by immunization, the tumors failed to regress due to an association with lack of CTL migration to the tumor sites (abstract). Thus, Gao *et al* teach that activation of peptide epitope-specific CTL is not an appropriate endopoint, and an estimation of efficacy based upon this factor is not predictive of actual efficacy of treatment *in vivo*.

Evidentiary reference Boon *et al* (Ann. Rev. Immunol. 2006, 24: 175-208) teach "Therapeutic vaccination of metastatic melanoma patients with these antigens [*i.e.,* melanoma antigens] is followed by tumor regressions in only a small minority of the patients (page 175, abstract). Boon *et al* further teach "In conclusion, therapeutic success following vaccination may not depend on the number of T cells produced directly by the vaccine, but rather on the production of a T cell clone with functional properties that enable it to migrate to the tumor and resist the local immunosuppressive environment long enough to initiate a regression process...To achieve therapeutic success, investigators will probably need to understand the cause of the local immunosuppression in the tumors and find counteracting agents. As stated above, the list of possible immunosuppressive agents present in tumors is considerable. But it will be important to find whether, for each type of tumor, there is a prevalent immunosuppressive agent. Just as many types of tumors have preferred oncogenic pathways that differ from one type of tumor to another, each type of tumor may also have preferred immunosuppressive processes that we must identify to achieve therapeutic success...Therapeutic vaccination of cancer has not yet proved to be effective enough to become a generally applied cancer treatment...We do not believe that melanoma patients suffer from a degree of general immunosuppression, which we believe is restricted to very late-stage patients who are not included in most studies...Therefore, the difference in the quality of the response would be due to a chance event determining, for instance, the functional properties of the unique or the few responder T cell clones elicited by the vaccine. In that case, it will be essential to understand what this crucial functional property is. At the other extreme, the antivaccine T cell responses would be similar in all patients, but the level of resistance of the tumors would vary considerably. In that case investigators would need to identify the main component of this resistance and find ways to counteract it." (especially pages 193-194).

In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief that clinical results for the present application are published in Clinical Cancer Res. 1005, 11(16): 5900-5911 (copy supplied by Applicant) and clearly shows the superior clinical effect of the present invention, and that claims 1 and 2 now recite that the peptide consists of the amino acid sequence as set forth in claims 1 and 2.

It is the Examiner's position that the instant claims are drawn to peptide consisting of "an" amino acid sequence of the SEQ ID NO recited in instant claim 1/inducer (not "the" amino acid sequence), vaccine recited in instant claim 7 or pharmaceutical composition thereof recited in instant claim 44, nor of the claimed peptide consisting of "an" amino acid sequence of SEQ ID NO: 10 recited in claim 2/kit comprising said peptide/inducer recited in instant claim 117, vaccine recited in instant claim 8 or pharmaceutical composition thereof recited in instant claim 45. It is the Examiner's further position that adequate written description must be present in the instant specification.

As a side issue, data in the said publication are for mixtures of peptides, some mixtures including one of SEQ ID NO: 1, 2 and/or 3 of the instant claims along with other tumor associated peptides from different tumor associated proteins, and a lack of correlation with immune responsiveness to said SEQ ID NO with clinical response since in some instances no immune response is noted to the said SEQ ID NO, but to other non-related peptides in the mixture, but clinical response is noted in terms of survival time for example, or in other instances, immune response is noted, but clinical outcome is not correlated positively with said response. In addition said publication states that "Increases in cellular or humoral responses specific to at least one of the vaccinated peptides were observed in the postvaccination samples of 15 of 21 patients regardless of the administration of prednisolone to the majority of patients. CTH responses were also observed in 12 of 21 patients. In contrast, no HLA class I-restricted cytotoxicity against glioma cells was observed, as measured by a 6-hour ^{51}Cr release assay, in either the prevaccination or the postvacination PBMCs. These results suggest that the administration of steroid hormone did not greatly influence the peptide-induced humoral responses, DTH responses, or cytokine production in response to an antigen, although it suppressed HLA class I-restricted cytotoxicity." (paragraph spanning pages 5909-5910). Said publication also teaches "Personalized peptide vaccinations were recommended for the further clinical study to malignant glioma patients." (abstract). In addition, said reference does not teach an internal positive control for HLA class I restricted CTL activity.

5. Claims 1-4, 7, 8, 44, 45 and 117 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

a. The specification does not disclose how to make and/or use the instant invention, of the claimed inducer of CTL recited in instant claims 3 and 4, wherein the said inducer *consists essentially of* a peptide of claim 1 or claim 2.

The specification does not disclose how to make and/or use the instant invention, ""inducers" of CTL that consist essentially of the peptide of claim 1 or claim 2, wherein said "inducers" include subsequences of the recited SEQ ID NO in claims 1 and 2 ("an" amino acid sequence of SEQ ID NO...), and including other undisclosed components ("consisting essentially of" a peptide of claim 1 or claim 2). The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the recited inducer can be made and/or used.

The specification discloses that SEQ ID NO: 11, 12 and 16 can be used as inducers for inducing CTL (page 16 at lines 5-25 and page 17 at lines 1-8).

The specification does not disclose the definition of "inducer."

Evidentiary reference Marchand *et al* (Exp. Opin. Biol. Ther. 1(3): 497-510, 2001, of record) teach "It is fair to say that in patients vaccinated with defined antigen, the immune responses induced have been so far very poor, if present. In some studies, immune responses were reported for some patients but without any correlation with the clinical responses. In addition, some patients with complete and long-term regressions of several melanoma metastases failed to mount a detectable response against the antigen present in the vaccine" (last paragraph at column 2 on page 505).

Evidentiary reference Paul (Fundamental Immunology, 2nd Edition, 1989, page 1006, column 1 at the second full paragraph, of record) teaches "It seems that both T and B memory cells are more readily stimulated to become effector cells compared to naïve cells..."
By using the term consisting essentially of,' the drafter signals that the invention necessarily includes the listed ingredients and is open to unlisted ingredients that do not materially affect the basic and novel properties of the invention. A consisting essentially of claim occupies a middle ground between closed claims that are written in a consisting of' format and fully open claims that are drafted in a comprising' format." PPG Industries v. Guardian Industries, 156 F.3d 1351, 1354, 48 USPQ2d 1351, 1353-54 (Fed. Cir. 1998). For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355

("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also In re Janakirama-Rao,317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1963). If an applicant contends that additional steps or materials in the prior art are excluded by the recitation of" consisting essentially of," applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention. In re De Lajarte, 337 F.2d 870, 143 USPQ 256 (CCPA 1964). See also MPEP § 2111.03. The claim as a whole, including all limitations found in the preamble(see Pac-Tec Inc. v. Amerace Corp., 903 F.2d 796, 801, 14 USPQ2d 1871, 1876 (Fed. Cir. 1990) (determining that preamble language that constitutes a structural limitation is actually part of the claimed invention), the transitional phrase, and the body of the claim, must be sufficiently supported to satisfy the written description requirement. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations. Lockwood,107 F.3d at 1572, 41 USPQ2d at 1966

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See *In re Wands* 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that claims 1 and 2 have been amended to recite that the peptide consists of the sequences set forth in claim 1 or claim 2, and that claims 3 and 4 have been amended to recite an inducer of CTL wherein the inducer consists essentially of the peptide of claim 1 or claim 2.

It is the Examiner's position that claims 1 and 2 have not been amended to recite that the peptide consists of "the" amino acid sequences set forth in claim 1 or claim 2, but rather to recited that the peptide consists of "an" amino acid sequence. It is the Examiner's further position that claims 3 and 4, as well as the other claims under examination, are not enabled for the reasons enunciated in the instant rejection.

b. The specification does not disclose how to make and/or use the instant invention, the claimed pharmaceutical composition recited in instant claims 44 and 45, said pharmaceutical composition comprising an effective amount for cancer treatment of at least one peptide of claim 1 or claim 2, nor the cancer vaccine recited in instant claims 7 and 8, said cancer vaccine comprising at least the peptide of claim 1 or claim 2. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the recited inducer can be made and/or used.

The instant claims encompass a pharmaceutical composition comprising an amount of at least one of the peptides of claim 1 or claim 2 effective for cancer treatment, or a cancer vaccine comprising the peptide of claim 1 or claim 2.

The specification discloses that SEQ ID NO: 1-3 are subsequence peptides of the lck protein that is over-expressed on adenocarcinoma cells or epithelial cancer cells in colon or small cell lung cancers bound to HLA-A2402, exhibited a CTL-activating ability of PBMC from a cancer patient (or PMBC from normal individuals when presented by HLA-A2402 on professional APC dendritic cells), as well as enhancing the production of IFN-γ by CTLs. The specification discloses that CTL induced by the said SEQ ID NO could recognize a tumor cell line (paragraph spanning pages 4-5, page 7 at lines 21-25, paragraph spanning pages 10-11, page 11 at lines 19-24, pages 12-13, Table 1 on page 28, Examples 4-6).

The specification further discloses that the amino acid sequence DYLRSV, common to both SEQ ID NO: 1 and 2, has a relevance to tumor rejection. The specification discloses searching for homologous sequences in other proteins, and testing subseqence 9-mer peptides from some of the tyrosine kinase proteins for binding to HLA-A2402 and for stimulating CTL (especially Examples 6-7). Larger 13-mer subsequences containing these peptides conform to the formula that is SEQ ID NO: 10 (Example 6).

There are no working examples of any *in vivo* method of treatment with the claimed peptides, and in addition, the specification does not provide a definition for effective treatment of cancer. The specification does not does not provide disclosure that administration of the peptide *in vivo* produces a CTL response that "treats" cancer.

The specification does not disclose working examples of any peptide recited in claim 1 or claim 2 used for treatment or for prophylaxis as a vaccine.

Evidentiary reference Marchand *et al* (Int. J. Cancer 20: 219-230, 1999, of record) teach "Considerable further progress is needed... before immunization with tumor-specific antigens recognized by T cells becomes an effective and generally applicable cancer therapy." (second to last sentence of article).

Evidentiary reference Marchand *et al* (Exp. Opin. Biol. Ther. 1(3): 497-510, 2001, of record) teach "It is fair to say that in patients vaccinated with defined antigen, the immune responses induced have been so far very poor, if present. In some studies, immune responses were reported for some patients but without any correlation with the clinical responses. In addition, some patients with complete and long-term regressions of several melanoma metastases failed to mount a detectable response against the antigen present in the vaccine." (last paragraph at column 2 on page 505).

Evidentiary reference Bodey *et al* (Anticancer Research 20: 2665-2676, 2000, of record) teach "while cancer vaccine trials have yielded tantalizing results, active immunotherapy has not yet become an established modality of anticancer therapy (page 2665 at column 2). Bodey *et al* further teach "the use of active specific immunotherapy for cancer is still in its infancy despite several decades of clinical and basic research" (page 2668 at column 2).

Evidentiary reference Gao *et al* (J. Immunother. 23: 643-653, 2000, of record) found that although anti-tumor CTL response was enhanced by immunization, the tumors failed to regress due to an association with lack of CTL migration to the tumor sites (abstract). Thus, Gao *et al* teach that activation of peptide epitope-specific CTL is not an appropriate endopoint, and an estimation of efficacy based upon this factor is not predictive of actual efficacy of treatment *in vivo*.

Evidentiary reference Boon *et al* (Ann. Rev. Immunol. 2006, 24: 175-208) teach "Therapeutic vaccination of metastatic melanoma patients with these antigens [*i.e.,* melanoma antigens] is followed by tumor regressions in only a small minority of the patients (page 175, abstract). Boon *et al* further teach "In conclusion, therapeutic success following vaccination may not depend on the number of T cells produced directly by the vaccine, but rather on the production of a T cell clone with functional properties that enable it to migrate to the tumor and resist the local immunosuppressive environment long enough to initiate a regression process...To achieve therapeutic success, investigators will probably need to understand the cause of the local immunosuppression in the tumors and find counteracting agents. As stated above, the list of possible immunosuppressive agents present in tumors is considerable. But it will be important to find whether, for each type of tumor, there is a prevalent immunosuppressive agent. Just as many types of tumors have preferred oncogenic pathways that differ from one type of tumor to another, each type of tumor may also have preferred immunosuppressive processes that we must identify to achieve therapeutic success...Therapeutic vaccination of cancer has not yet proved to be effective enough to become a generally applied cancer treatment...We do not believe that melanoma patients suffer from a degree of general immunosuppression, which we believe is restricted to very late-stage patients who are not included in most studies...Therefore, the difference in the quality of the response would be due to a chance event determining, for instance, the functional properties of the unique or the few responder T cell clones elicited by the vaccine. In that case, it will be essential to

understand what this crucial functional property is. At the other extreme, the antivaccine T cell responses would be similar in all patients, but the level of resistance of the tumors would vary considerably. In that case investigators would need to identify the main component of this resistance and find ways to counteract it." (especially pages 193-194).

Evidentiary reference the Merck Manual (of record) teaches that a vaccine is a suspension of whole or fractionated bacteria or viruses that have been rendered nonpathogenic and is given to induce an immune response and prevent subsequent disease.

Evidentiary reference Encyclopedia Brittanica Online (of record) defines vaccine as a suspension of weakened, killed, or fragmented microorganisms or toxins or of antibodies or lymphocytes that is administered primarily to prevent disease.

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See *In re Wands* 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that claims 1 and 2 have been amended to recite that the peptide consists of the sequences set forth in claim 1 or claim 2, and that claims 3 and 4 have been amended to recite an inducer of CTL wherein the inducer consists essentially of the peptide of claim 1 or claim 2.

It is the Examiner's position that claims 1 and 2 have not been amended to recite that the peptide consists of "the" amino acid sequences set forth in claim 1 or claim 2, but rather to recited that the peptide consists of "an" amino acid sequence. It is the Examiner's further position that claims 3 and 4, as well as the other claims under examination, are not enabled for the reasons enunciated in the instant rejection.

c. The specification does not disclose how to make and/or use the instant invention, the claimed peptide consisting of "an" amino acid sequence of the SEQ ID NO recited in instant claim 1/inducer, vaccine recited in instant claim 7 or pharmaceutical composition thereof recited in instant claim 44, nor of the claimed peptide consisting of "an" amino acid sequence of SEQ ID NO: 10 recited in claim 2/kit comprising said peptide/inducer recited in instant claim 117, vaccine recited in instant claim 8 or pharmaceutical composition thereof recited in instant claim 45. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the recited peptide can be made and/or used.

The instant claims encompass: (1) a peptide consisting of a subsequence of one of the SEQ ID NO recited in instant claim 1 ("an" amino acid sequence of SEQ ID NO....), said subsequence does not bind to HLA-A*2402 and elicit an immune response, and that in addition may comprise additional undisclosed flanking regions for the inducers of claims 3 and 4, vaccine and pharmaceutical composition thereof, (2) a peptide consisting of a subsequence of SEQ ID NO: 10 that is not one of SEQ ID NO: 1, 2, 4-9, but is rather a subsequence of SEQ ID NO: 10 that does not bind to HLA-A*2402 and elicit an immune response, vaccine and pharmaceutical composition thereof.

The specification discloses that SEQ ID NO: 1-3 are subsequence peptides of the Lck protein that is over-expressed on adenocarcinoma cells or epithelial cancer cells in colon or small cell lung cancers bound to HLA-A2402, exhibited a CTL-activating ability of PBMC from a cancer patient (or PMBC from normal individuals when presented by HLA-A2402 on professional APC dendritic cells), as well as enhancing the production of IFN-γ by CTLs. The specification discloses that CTL induced by the said SEQ ID NO could recognize a tumor cell line (paragraph spanning pages 4-5, page 7 at lines 21-25, paragraph spanning pages 10-11, page 11 at lines 19-24, pages 12-13, Table 1 on page 28, Examples 4-6).

The specification further discloses that the amino acid sequence DYLRSV, common to both SEQ ID NO: 1 and 2, has a relevance to tumor rejection. The specification discloses searching for homologous sequences in other proteins, and testing subseqence 9-mer peptides from some of the tyrosine kinase proteins for binding to HLA-A2402 and for stimulating CTL (especially Examples 6-7). Larger 13-mer subsequences containing these peptides conform to the formula that is SEQ ID NO: 10 (Example 6).

There are no working examples of any smaller subsequences of SEQ ID NO: 1-3 that are shorter than 9 or 10 amino acid residues in length, or that do not contain one of SEQ ID NO: 1, 2, 4-9, and/or that contain additional undisclosed flanking amino acid sequence (inducer consisting essentially of a peptide of claim 1 or claim 2). There are no working examples of any peptide consisting of the sequence of SEQ ID NO: 10 that bind to an HLA class I molecule and elicit a CTL response, though smaller 9 or 10-mer

subsequences of the optimal length to bind to an HLA class I molecule are disclosed in the instant specification to stimulate CTL *in vitro*.

It is unpredictable that the claimed peptide would bind to HLA and would be recognized by CTL, *i.e.,* be a T cell epitope. The specification provides no evidence that the peptide consisting of some subsequence of one of SEQ ID NO: 1-3 or 10: (1) would bind to an MHC molecule either by itself or when present in a longer peptide of unknown length and flanked by amino acid sequences not present in the antigenic protein of origin, (2) or would be recognized by CTL. The specification provides no evidence that the peptide consisting of SEQ ID NO: 10 (13-mer peptide) would bind to an HLA class I molecule or would be recognized by CTL.

In addition, the art recognizes that flanking sequences influence the processing and presentation of CTL epitopes (Eisenlohr *et al*, Shastri *et al*, Bergmann *et al*, Wang *et al*, Perkins *et al*, Theoboald *et al* and Gileadi *et al*, all of record) and that immunodominance can be affected by the context of the epitope within the protein molecule and that junctional neoepitopes can be created (Perkins *et al*, of record) or that immunodominant epitopes can be completely silenced by contiguous sequences (Wang *et al*, of record). An undue amount of experimentation would be involved in determining longer peptides from the many possibilities that would be capable of binding to HLA and being recognized by CTL.

The art recognizes that for a peptide to be a T cell epitope, the length of the peptide is important for binding to HLA (along with the presence of anchor (or "motif") amino acid residues present within the peptide). The peptides that bind to class I molecules have a predominant length, *i.e.,* a minimum of 8 or 9 amino acid residues for a class I MHC restricted T cell epitope peptide. A primary factor for this is that amino acid residues at the amino- and carboxy-termini of peptides binding to class I molecules interact with conserved amino acid residues in pockets ("A","F") located at opposite ends of the binding groove of the class I molecule, giving rise to a common orientation of the peptides in the binding site (Engelhard at page 14, column 1, lines 16-27, of record). Thus, the amino acid residues at the peptides' termini make a network of hydrogen bonds with conserved residues on the sides and bottom of the peptide binding groove of class I molecules. These interactions are important for holding the peptides in the binding groove and for stabilizing the complex (Guo *et al* at page 366, column 1 lines 1-10, of record.) "...the preferred length (of the peptide) is determined by the minimum amount of peptide required to span the center of the binding site and optimize the interactions at the ends," but that the predominant length is 9 amino acid residues (Engelhard at page 14, column 1, lines 23-27, of record).

Evidentiary reference Marchand *et al* (Int. J. Cancer 20: 219-230, 1999, of record) teach "Considerable further progress is needed... before immunization with tumor-specific antigens recognized by T cells becomes an effective and generally applicable cancer therapy." (second to last sentence of article).

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understand what this crucial functional property is. At the other extreme, the antivaccine T cell responses would be similar in all patients, but the level of resistance of the tumors would vary considerably. In that case investigators would need to identify the main component of this resistance and find ways to counteract it." (especially pages 193-194).

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There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that claims 1 and 2 have been amended to recite that the peptide consists of the sequences set forth in claim 1 or claim 2, and that claims 3 and 4 have been amended to recite an inducer of CTL wherein the inducer consists essentially of the peptide of claim 1 or claim 2.

It is the Examiner's position that claims 1 and 2 have not been amended to recite that the peptide consists of "the" amino acid sequences set forth in claim 1 or claim 2, but rather to recited that the peptide consists of "an" amino acid sequence. It is the Examiner's further position that claims 3 and 4, as well as the other claims under examination, are not enabled for the reasons enunciated in the instant rejection.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4, 7, 8, 44, 45 and 117 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1 and 2 are indefinite in the recitation of "consisting of an" amino acid sequence of SEQ ID NO because it is not clear what is meant, *i.e.*, what the metes and bounds of the claims are.

b. Claims 3 and 4 are indefinite in the recitation of "An inducer of cytotoxic T lymphocytes" because it is not clear what is meant. The instant specification does not disclose the definition of "An inducer of cytotoxic T lymphocytes."

c. Claims 3 and 4 are indefinite in the recitation of "consists essentially of a peptide of claim" because it is not clear what is meant, *i.e.,* what the metes and bounds of the claim are. In addition said claims are indefinite because the inducer of claims 3 and 4 is broader than the peptide of claims 1 and 2 that consist of an amino acid sequence of the recited SEQ ID NO.

d. Claim 117 is indefinite in the recitation of "A reagent kit for screening a compound comprising at least one peptide according to claim 2" because it is not clear what is meant, *i.e.,* if the kit contains undisclosed ingredients for screening a compound that comprises at least one peptide according to claim 2, or if the kit contains at least one peptide according to claim 2.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that claims 1 and 2 now recite "consisting of" and claims 3 and 4 recite "consisting essentially of", and therefore, these peptides are clearly described in the present application and would be definite to one of skill in the art.

It is the Examiner's position that the claims are indefinite for the reasons enunciated in the instant rejection, and that claims 1 and 2 recite consisting of "an amino acid sequence."

8. For the purpose of prior art rejections, the filing date of the instant claims 1-4, 7, 8, 44, 45 and 117 are deemed to be the filing date of the PCT/JP00/05220, *i.e.,* 8/3/00.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/22255 A1 (of record).

WO 97/22255 A1 teaches a peptide comprising SEQ ID NO: 3 of the instant claims (especially page 11 at lines 25-26, Figure 5, page 18 at lines 30-33 and page 46 at lines 30-35).

Claim 3 is included in this rejection because the recitation of "wherein the inducer consists essentially of a peptide of claim 1" opens the claim to read on flanking sequences for SEQ ID NO: 3.

Claim 3 is also included in this rejection because while the art reference is silent as to whether the composition is an inducer of CTL, the claimed peptide appears to be the same as that of the prior art reference, absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the peptide of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252,195 USPQ 430 (CCPA 1977).

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that the reference does not teach the claimed sequences specifically recited.

It is the Examiner's position that the art reference does meet the claim limitations for the reasons enunciated in the instant rejection.

11. Claims 3 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,635,623 B1 (of record).

US 6,635,623 B1 discloses a peptide comprising SEQ ID NO: 1 and 2 of the instant claims, wherein SEQ ID NO: 1 and 2 are subsequences of SEQ ID NO: 10 (SEQ ID NO: 74 of the art reference).

Claims 3 and 4 are included in this rejection because the recitation of "wherein the inducer consists essentially of a peptide of claim" 1 or 2 opens the claim to read on flanking sequences for SEQ ID NO: 1 and 2.

Claims 3 and 4 are also included in this rejection because while the art reference is silent as to whether the composition is an inducer of CTLs, the claimed peptide appears to be the same as that of the prior art reference, absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant

to show a distinction between the peptide of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252,195 USPQ 430 (CCPA 1977).

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that the reference does not teach the claimed sequences specifically recited.

It is the Examiner's position that the art reference does meet the claim limitations for the reasons enunciated in the instant rejection.

12. Claims 3 and 4 are rejected under 35 U.S.C. 102(e) as being anticipated by US 5,432,076 (of record).

US 5,432,076 discloses a peptide comprising SEQ ID NO: 1 and 2 of the instant claims (the sequence appearing at column 5, lines 23-27 of the art reference).

Claims 3 and 4 are included in this rejection because the recitation of "wherein the inducer consists essentially of a peptide of claim" 1 or 2 opens the claim to read on flanking sequences for SEQ ID NO: 1 and 2.

Claims 3 and 4 are also included in this rejection because while the art reference is silent as to whether the peptide is an inducer of CTLs, the claimed peptide appears to be the same as that of the prior art reference, absent a showing of differences. Since the Patent Office does not have the facilities for examining and comparing the composition of the instant invention to those of the prior art, the burden is on Applicant to show a distinction between the pharmaceutical composition of the instant invention and that of the prior art. See *In re Best*, 562 F.2d 1252,195 USPQ 430 (CCPA 1977). Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's amendment filed 11/17/06, in brief, that the reference does not teach the claimed sequences specifically recited.

It is the Examiner's position that the art reference does meet the claim limitations for the reasons enunciated in the instant rejection.

13. Claim 1 is objected to because of the following informalities: Claim 1 recites SEQ ID NO that are in non-elected groups. Appropriate correction is required.

14. No claim is allowed.

15. The information disclosure statement filed 6/14/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Specifically, the Form 1449 filed 6/14/02 does not provide a copy of the IPER listed on said Form 1449.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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